

**REMARKS**

**I. Amendments to the Claims**

Claims 1-11 are all the claims currently pending in the application. Of these claims, claims 3-6 are withdrawn from consideration. After entry of this amendment, claims 3-13 will be all the claims pending in this application.

Claims 1 and 2 have been canceled, without prejudice to refiling.

Claims 3-6, which were dependant on claim 1, have been amended to include the subject matter of claim 1.

Claim 7 has been amended to recite “a method for treatment” rather than “a method for treatment and/or prevention,” and to delete allergic disease, asthma, allergic rhinitis, atopic dermatitis, urticaria, contact dermatitis, inflammatory bowel disease, ulcerative colitis, Crohn disease, and eosinophilic pneumonia.

Claims 8-10 have been canceled, without prejudice to refiling.

Claim 12, which recites the method of claim 7 wherein k is 1 and m is 2 in formula(I) has been added.

Claim 13, which recites the method of claim 7 or 12 wherein n is 0 in formula (I), has also been added.

**II. Double Patenting Rejection**

At paragraphs 1 and 2 on page 2 of the Office Action, claims 1, 2, and 7-11 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable

over claims 12-26 of Shiota et al., U.S. Patent No. 6,451,842, assigned to Dupont Pharmaceuticals Co. and Teijin Ltd.

As in the previous Office Action, the Examiner contended that although the conflicting claims are not identical, they are not patentably distinct from each other, because the '842 patent claims a method of inhibiting the binding of chemokine to the receptor of target cells by using compounds or their salts that substantially overlap with the compounds employed herein, and encompasses the elected species. The Examiner further contended that although '842 does not expressly claim inhibition of CCR3 or a method of treating CCR3-related disease, administering the compounds to a subject would inherently inhibit CCR3 and prevent disorders associated with CCR3.

First, claims 1, 2, and 8-10 have been canceled, making this rejection moot as to those claims.

In addition, Applicants respectfully traverse the double patenting rejection with respect to claims 7 and 11, and once again submit that a double-patenting rejection does not apply where, as in this case, the patent principally underlying the rejection is prior art (see page 15 of the April 16, 2004 response to the previous Office Action in the present application).

Furthermore, for reasons discussed below, Applicants submit that the disclosure of the '842 patent does not teach or suggest present claims 7 or 11.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

### **III. Claim Rejections Under 35 U.S.C. § 112 - Enablement**

At pages 2 and 3 of the Office Action, claims 1, 2, and 7- 11 were rejected under 35 U.S.C. § 112, first paragraph, as failing to meet the enablement requirement.

Again, claims 1, 2, and 8-10 have been canceled, making this rejection moot as to those claims.

With respect to claims 7 and 11, the Examiner acknowledged that the specification discloses that the claimed compositions are CCR3 antagonistic and may be useful in alleviating or suppressing the symptoms of diseases associated with CCR3. However, the Examiner contended that the specification fails to adequately teach how to use the claimed methods to prevent such diseases.

Claims 7 and 11 have been amended by deleting the phrase “and/or prevention” from the claims. Thus, Applicants submit that claims 7 and 11 are fully enabled, and respectfully request reconsideration and withdrawal of this rejection.

### **IV. Claim Rejections 35 U.S.C. § 103 - Obviousness**

#### ***A. Shiota et al.***

At pages 4 and 5 of the Office Action, claims 1, 2, and 7- 11 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Shiota et al. (US 6,451,842, or WO 99/25686).

Specifically, the Examiner contended that Shiota teaches therapeutical compounds with a general formula essentially identical to Teijin’s formula (I). Furthermore, the general formula

taught by Shiota encompasses the particular species elected. The Examiner also contended that Shiota discloses that the compounds are useful for treating and/or preventing various disorders, including asthma and Crohn's disease (citing page 1 of the '686 patent). Finally, the Examiner contended that although Shiota does not teach interaction of the recited compounds with CCR3, it is well settled patent law that elucidating the mode of action does not impart patentable moment to otherwise old and obvious subject matter.

Once again, claims 1, 2, and 8-10 have been canceled, making this rejection moot as to those claims.

Regarding claims 7 and 11, these claims have been amended to delete allergic disease, asthma, allergic rhinitis, atopic dermatitis, urticaria, contact dermatitis, inflammatory bowel disease, ulcerative colitis, Crohn disease, and eosinophilic pneumonia. Applicants submit that one of ordinary skill in the art at the time of the instant invention would not have reasonably expected the claimed compounds to be useful for treating the diseases recited in amended claims 7 and 11, namely allergic conjunctivitis, eosinophilia, eosinophilic gastroenteritis, eosinophilic enteropathy, eosinophilic fasciitis, eosinophilic granuloma, eosinophilic pustular folliculitis, eosinophilic leukemia, and Acquired Immuno-Deficiency Syndrome (AIDS), for at least the following reasons.

First, as noted in the Amendment filed April 16, 2004 in this application, Shiota does not teach or suggest inhibition of CCR3 activity or even interaction of compounds with CCR3 receptors. Furthermore, the reference does not teach or suggest use of compounds for treating allergic diseases or any of the other CCR3-related diseases specified in claims 7-11.

The target diseases disclosed by Shiota all involve the binding of chemokines to particular chemokine receptors on the cell surface. Specifically, the chemokine receptors described by Shiota are CCR1, CCR2A, and CCR2B, which interact with chemokines MIP-1 $\alpha$  and/or MCP-1. The chemokines described in the reference are not ligands of CCR3. In addition, the receptors described in the reference do not interact with the CCR3 ligand eotaxin. Furthermore, compounds tested in Example 2043 of Shiota were shown to inhibit the binding of MIP-1 $\alpha$  (see column 689), while the compounds tested in Examples 2044 and 2045 were shown to inhibit MCP 1 binding (columns 691-695).

Applicants note also that the amino acid sequences of CCR1 and CCR2 have very low homology to the sequence of CCR3 (about 60% and 50% identity, respectively), thus one of ordinary skill in the art would not expect compounds that bind to CCR1 and CCR2 to also bind to CCR3.

Accordingly, one of ordinary skill in the art at the time of the instant invention would not have reasonably expected the compounds of Shiota to be useful for treating CCR3-related diseases. Thus, use of the compounds recited in the present claims for inhibiting CCR3, and for treating allergic conjunctivitis, eosinophilia, eosinophilic gastroenteritis, eosinophilic enteropathy, eosinophilic fasciitis, eosinophilic granuloma, eosinophilic pustular folliculitis, eosinophilic leukemia, and AIDS, is not taught or suggested by Shiota.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection.

***B. Rogers et al.***

At pages 4 and 5 of the Office Action, claims 1, 2, and 7-11 were rejected under 35 U.S.C. §103(a) as being unpatentable over Rogers et al. (US 6,166,015).

Specifically, the Examiner contended that the general formula (I) in Rogers substantially overlaps in scope with the general formula of the present invention, particularly where A is 9I) - N(R<sup>2</sup>)C(O)- and B is -C(O)- or -S(O)<sub>n</sub>-. The Examiner also contended that Rogers teaches a method of treating CCR3 associated disorders, such as asthma, by administering the compounds to patients.

Because claims 1, 2, and 8-10 have been canceled, this rejection is moot as to those claims.

As noted above, claims 7 and 11 have been amended to delete allergic disease, asthma, allergic rhinitis, atopic dermatitis, urticaria, contact dermatitis, inflammatory bowel disease, ulcerative colitis, Crohn disease, and eosinophilic pneumonia.

Applicants submit that one of ordinary skill in the art at the time of the instant invention would not have reasonably expected the claimed compounds to be useful for treating the diseases recited in amended claims 7 and 11 in light of Rogers, for at least the following reasons.

First, as noted in the April 16, 2004 Amendment, the compounds recited in the instant claims are not encompassed by the compounds of general formula (I) in Rogers. Furthermore, the general formula disclosed by Rogers does not encompass compound 2296, the particular species elected by Applicants in the Response to Restriction and Election of Species filed July 25, 2003. Specifically, compound 2296 differs from the general formula (I) disclosed in Rogers

at least in that the methylene group between A and the 5-membered ring containing Z in Rogers is not present in the elected species.

In addition, new claim 13 recites that n is 0. Rogers does not teach the compounds of claim 13, where n is 0.

Because Rogers does not teach or suggest the structure of the compounds recited in the present claims, one of skill in the art would not have reasonably expected the compounds to have CCR3 receptor antagonist activity. In addition, Rogers does not teach or suggest that the compounds would be useful for treating any of the diseases recited in claims 7 and 11. Therefore, use of the compounds to treat and prevent the recited diseases is not obvious in light of Rogers.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

## **VI. Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

AMENDMENT UNDER 37 C.F.R. § 1.116  
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